L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 202409-33-4 REGISTRY

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 5-Chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine

CN Arcoxia

CN Etoricoxib

CN MK 0663

CN MK 663

FS 3D CONCORD

MF C18 H15 C1 N2 O2 S

CI COM

SR CA

LC STN Files: ADISINSIGHT, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(*File contains numerically searchable property data)

DT.CA CAplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

220 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

223 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
L2
     26839-75-8 REGISTRY
RN
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
CN
     thiadiazol-3-yl]oxy]-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     1,2,5-Thiadiazole, 2-propanol deriv.
CN
     2-Propanol, 1-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-
     y1)oxy]-, (S)-(-)-(8CI)
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
CN
     thiadiazol-3-yl]oxy]-, (S)-
OTHER NAMES:
     (-)-S-Timolol
CN
CN
     (-)-Timolol
CN
     (S)-Timolol
CN
     1-Timolol
CN
     L-Timolol
CN
     Oftensin
CN
     Timolol
FS
     STEREOSEARCH
     131628-37-0, 194288-09-0
DR
     C13 H24 N4 O3 S
MF
CI
     COM
LC
                  ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
     STN Files:
       BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST,
       CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT,
       IFIUDB, IMSCOSEARCH, IMSPATENTS, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR,
       PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
                      EINECS**, NDSL**, TSCA**, WHO
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
      CAplus document type: Conference; Dissertation; Journal; Patent
DT.CA
       Roles from patents: ANST (Analytical study); BIOL (Biological study);
RL.P
       MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP
       (Properties); RACT (Reactant or reagent); USES (Uses)
       Roles for non-specific derivatives from patents: BIOL (Biological
RLD.P
       study); PREP (Preparation); USES (Uses)
       Roles from non-patents: ANST (Analytical study); BIOL (Biological
RL.NP
       study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PRP (Properties); RACT (Reactant or reagent)
```

Absolute stereochemistry. Rotation (-).

^{**}PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

- 1315 REFERENCES IN FILE CA (1907 TO DATE)
- 22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1321 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=>

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
L3
RN
     26921-17-5 REGISTRY
CN
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
     thiadiazol-3-yl]oxy]-, (2S)-, (2Z)-2-butenedioate (1:1) (salt) (9CI) (CA
OTHER CA INDEX NAMES:
     1,2,5-Thiadiazole, 2-propanol deriv.
CN
     2-Propanol, 1-(tert-butylamino)-3-[(4-morpholino-1,2,5-thiadiazol-3-
     y1)oxy]-, (-)-, maleate (1:1) (salt) (8CI)
     2-Propanol, 1-[(1,1-dimethylethyl)amino]-3-[[4-(4-morpholinyl)-1,2,5-
     thiadiazol-3-yl]oxy]-, (S)-, (Z)-2-butenedioate (1:1) (salt)
OTHER NAMES:
     (-)-Timolol maleate
CN
     (S)-(-)-Timolol maleate
CN
CN
     (S)-Timolol hydrogen maleate
CN
     Aquanil
     Betim
CN
CN
     Betime
CN
     Blocadren
CN
     Blocanol
CN
     Istalol
CN
     L-Timolol maleate
CN
     1-Timolol maleate
CN
     MK 950
CN
     Optimol
CN
     Proflax
CN
     Rysmon TG
CN
     Temserin
CN
     Tenopt
CN
     Timabak
CN
     Timacar
CN
     Timacor
CN
     Timolol hydrogen maleate
CN
     Timolol LA
     Timolol maleate
CN
CN
     Timoptic
CN
     Timoptol
     Timoptol XE
CN
CN
     Timorom
CN
     WP 934
FS
     STEREOSEARCH
DR
     131628-38-1, 30166-36-0, 116475-10-6
MF
     C13 H24 N4 O3 S . C4 H4 O4
CI
     COM
                ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
LC
     STN Files:
       BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB,
       IMSPATENTS, IPA, MRCK*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*,
       TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
                     EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P
       Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
       (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P
       Roles for non-specific derivatives from patents: BIOL (Biological
       study); USES (Uses)
       Roles from non-patents: ANST (Analytical study); BIOL (Biological
RL.NP
       study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP
       (Properties); RACT (Reactant or reagent); USES (Uses)
```

CM 2

CRN 26839-75-8

CMF C13 H24 N4 O3 S

Absolute stereochemistry. Rotation (-).

CM 2

CRN 110-16-7

=> d 111 1-10 bib, kwic

- L11 ANSWER 1 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1987:233574 BIOSIS
- DN PREV198783121744; BA83:121744
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- AU GALLAGHER R M [Reprint author]; STAGLIANO R A; SPORAZZA C
- CS MED CENTER FOR HEADACHE, 513 SOUTH LENOLA ROAD, MOORESTOWN, NEW JERSEY 08057, USA
- SO Headache, (1987) Vol. 27, No. 2, pp. 84-86. CODEN: HEADAE. ISSN: 0017-8748.
- DT Article
- FS BA
- LA ENGLISH
- ED Entered STN: 22 May 1987 Last Updated on STN: 22 May 1987
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- SO Headache, (1987) Vol. 27, No. 2, pp. 84-86. CODEN: HEADAE. ISSN: 0017-8748.
- Timolol maleate, a beta blocker, has been shown to reduce the frequency of common migraine headache in clinical trials. An analysis of 116 patients treated prophylactically for common migraine with timolol maleate 10-30 mg·per day was conducted. There were 35 males and 81 females ranging in age from 19.
 . . patients (20%) showed < 25% improvement, and 4 patients (3%) discontinued because of side effects. This limited study suggests that timolol maleate may be of benefit in the treatment of some migraine patients.
- RN 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 2 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1986:431759 BIOSIS
- DN PREV198631097571; BR31:97571
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- AU GALLAGHER R M [Reprint author]; STAGLIANO R A
- CS MOORESTOWN, NJ, USA
- Headache, (1986) Vol. 26, No. 6, pp. 312.
 Meeting Info.: TWENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION
 FOR THE STUDY OF HEADACHE, CHICAGO, ILL., USA, JUNE 27-29, 1986. HEADACHE.
 CODEN: HEADAE. ISSN: 0017-8748.
- DT Conference; (Meeting)
- FS BR
- LA ENGLISH
- ED Entered STN: 25 Oct 1986 Last Updated on STN: 25 Oct 1986
- TI TIMOLOL MALEATE A BETA BLOCKER IN THE TREATMENT OF COMMON MIGRAINE HEADACHE.
- SO Headache, (1986) Vol. 26, No. 6, pp. 312.
 Meeting Info.: TWENTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION
 FOR THE STUDY OF HEADACHE,. . .
- RN 26921-17-5 (TIMOLOL MALEATE)
- L11 ANSWER 3 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
- AN 1982:232842 BIOSIS
- DN PREV198274005322; BA74:5322

plud

BLOCADREN TIMOLOL MALEATE IN THE TREATMENT OF MIGRAINE ΤI PILOT STUDY. LOVLAND B [Reprint author] ΑU LOKKEGARDEN LEGEKONTOR, 1400 SKI CS Tidsskrift for den Norske Laegeforening, (1981) Vol. 101, No. SO 29, pp. 1645-1646. CODEN: TNLAAH. ISSN: 0029-2001. DTArticle FS BA LΑ NORWEGIAN BLOCADREN TIMOLOL MALEATE IN THE TREATMENT OF MIGRAINE TΙ PILOT STUDY. Tidsskrift for den Norske Laegeforening, (1981) Vol. 101, No. 29, pp. 1645-1646. CODEN: TNLAAH. ISSN: 0029-2001. Patients [23] with migraine were, after a wash-out period of 8 AΒ wk, treated with blocadren (timolol maleate) for 16 wk. Treatment efficacy was primarily evaluated as a reduction in the number of attacks per month and. 26921-17-5 (BLOCADREN) RN 26921-17-5 (TIMOLOL MALEATE) L11 ANSWER 4 OF 10 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN 1980:253770 BIOSIS ΑN PREV198070046266; BA70:46266 DN THERAPEUTIC USE OF BETA BLOCKERS IN GENERAL PATHOLOGY RHEUMATOLOGY TINEUROLOGY AND OPHTHALMOLOGY. BOUVENOT G [Reprint author]; BARTOLIN R; ESCANDE M; DELBOY C ΑU SERV MED INTERN, HOTEL DIEU, 13224 MARSEILLE CEDEX 1, FR CS Therapie (London/Paris), (1980) Vol. 35, No. 1, pp. 61-82. SO CODEN: THERAP. ISSN: 0040-5957. DTArticle FS BA FRENCH T.A Therapie (London/Paris), (1980) Vol. 35, No. 1, pp. 61-82. SO CODEN: THERAP. ISSN: 0040-5957. . of Sudek's atrophy and spasmophilia with tachycardia. In neurology, AB. β -blockers are interesting in 60-80% of cases of all types of migraine; they decrease the amplitude of senile tremor but they are inactive on the parkinsonian tremor. In ophthalmology, the use of. IT Miscellaneous Descriptors HUMAN CARDIO VASCULAR SYSTEM TIMOLOL MALEATE AUTONOMIC-DRUG OPHTHALMIC-DRUG SUDEKS ATROPHY SPASMOPHILIA TACHY CARDIA MIGRAINE SENILE TREMOR PARKINSONIAN TREMOR OPEN ANGLE GLAUCOMA PSYCHIATRY EYE DROP PHARMACODYNAMICS RN 26921-17-5 (TIMOLOL MALEATE) ANSWER 5 OF 10 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN T.11 ΑN 1998:28538277 BIOTECHNO Report to the Danish committee on adverse drug reactions TIINDBERETNING TIL BIVIRKNINGSNAEVNET Bivirkningsnaevn, Sundhedsstyrelsen, Frederikssundsvej 387, DK-2700 CS Bronshoj. Ugeskrift for Laeger, (23 NOV 1998), 160/48 (6996-6998), 20 SO reference(s) CODEN: UGLAAD ISSN: 0041-5782

Ugeskrift for Laeger, (23 NOV 1998), 160/48 (6996-6998), 20

DT

CY

LA

SO

Journal; Note

Denmark Danish reference(s)
CODEN: UGLAAD ISSN: 0041-5782

RN. . . 104632-26-0; (lepirudin) 138068-37-8; (sodium dihydrogen phosphate) 7558-80-7, 7632-05-5; (brimonidine) 59803-98-4; (lamivudine) 134678-17-4, 134680-32-3; (zidometacin) 62851-43-8; (mercaptamine) 156-57-0, 60-23-1; (navelbine) 71486-22-1; (timolol maleate) 26921-17-5; (dorzolamide) 130693-82-2; (ibandronic acid) 114084-78-5, 138844-81-2, 138926-19-9; (mizolastine) 108612-45-9; (prostavasin) 55648-20-9; (prostaglandin el) 745-65-3; (montelukast) 151767-02-1, 158966-92-8; (hyaluronic acid) 31799-91-4,. . .

L11 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:215996 CAPLUS

DN 138:8296

TI Facilitated delivery of timolol maleate by iontophoresis

AU Saraf, Swarnlata; Jain, S.; Dixit, V. K.

CS B.R. Nahata College of Pharmacy, 458 001, India

SO Indian Drugs (2001), 38(7), 376-379 CODEN: INDRBA; ISSN: 0019-462X

PB Indian Drug Manufacturers' Association

DT Journal

LA English

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

SO Indian Drugs (2001), 38(7), 376-379 CODEN: INDRBA; ISSN: 0019-462X

AΒ Timolol maleate (TM) is a β -adrenergic blocker used in cardiovascular and respiratory complications like hypertension, glaucoma, angina pectoris, myocardial infarction and migraine. The iontophoretic technique has been used to enhance the delivery of TM through skin. It is a technique, which permeate ionic form of drugs across the membrane by passing the current through an electrolyte. Iontophoretic delivery of drugs is affected by physico-elec. factors like initial drug concentration, pH, ionic strength, and frequency. These factors were aimed to be optimized for the iontophoretic delivery of TM through the skin. The passive and iontophoretic drug skin permeation studies were conducted by 2-chambered horizontal diffusion cells and human cadaver skin. The iontophoretic permeation through skin was dependent on the ionic species of drug. By optimizing the pH and ionic strength of donor solution and frequency of current the iontophoretic permeability of TM can be enhanced.

L11 ANSWER 7 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 96005820 EMBASE

DN 1996005820

```
Medications used to prevent migraine headaches and their
TI
     potential ocular adverse effects.
ΑU
     Doughty M.J.; Lyle W.M.
     Department of Vision Science, Glasgow-Caledonian University, Cowcaddens
CS
     Road, Glasgow G4 OBA, United Kingdom
     Optometry and Vision Science, (1995) 72/12 (879-891).
SO
     ISSN: 1040-5488 CODEN: OVSCET
CY
     United States
     Journal; Article
DT
             Neurology and Neurosurgery
FS
     800
             Ophthalmology
     012
             Drug Literature Index
     037
     038
             Adverse Reactions Titles
LA
     English
SL
     English
     Medications used to prevent migraine headaches and their
TI
     potential ocular adverse effects.
     Optometry and Vision Science, (1995) 72/12 (879-891).
SO
     ISSN: 1040-5488 CODEN: OVSCET
          . present a detailed review of the medications used in the USA,
AB
     Canada, and the United Kingdom for the prevention of migraine
     and the potential ocular adverse effects associated with the use of these
     medications. Those drugs that are administered for the purpose of reducing
     the frequency or severity of migraine attacks are classified
     according to whether they act on the cerebral vasculature primarily at
     serotonin (5-HT2) receptors (e.g., methysergide, cyproheptadine, and
     pizotyline), beta adrenergic (primarily beta-2) receptors (e.g.,
     propranolol and timolol), via central nervous system (CNS)
     adrenergic (alpha-2) receptors (e.g., clonidine), or calcium channels
     (e.g., flunarizine). The roles and mechanisms of action of tricyclic
     antidepressants (e.g., amitriptyline) and non-steroidal anti-inflammatory
     drugs (NSAIDs) in the prophylactic management of migraine are
     also discussed, along with possible pharmacogenetic differences in the
     kinetics of action of some of these drugs. The general.
     Medical Descriptors:
CT
     *eye disease: ET, etiology
     *eye disease: SI, side effect
       *migraine: PC, prevention
       *migraine: DT, drug therapy
     article
     conjunctivitis: SI, side effect
     diplopia: SI, side effect
     drug contraindication
     drug mechanism
     drug safety
     dry eye: SI, side effect
     food composition
     gastrointestinal symptom: SI, side.
     . . 21829-25-4; (phenethylamine) 64-04-0; (pizotifen) 15574-96-6;
RN.
      (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6;
      (reserpine) 50-55-5, 8001-95-4; (serotonin) 50-67-9; (timolol) 26839-75-8;
      (timolol maleate) 26921-17-5; (tryptamine) 343-94-2, 61-54-1;
      (tyramine) 51-67-2, 60-19-5
     ANSWER 8 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
L11
     on STN
AN
     85050077 EMBASE
     1985050077
DN
      [Antimigraine agents].
TI
     ANTIMIGRAINEUX.
     Rascol A.; Fanchamps A.
ΑU
```

```
Service de Neurologie, CHU Purpan, 31059 Toulouse Cedex, France
CS
     Semaine des Hopitaux, (1984) 60/44-45 (3137-3161).
SO
     CODEN: SHPAAI
CY
     France
DT
     Journal
FS
     038
             Adverse Reactions Titles
     037
             Drug Literature Index
     800
             Neurology and Neurosurgery
     030
             Pharmacology
     French
LΑ
     English
SL
     Semaine des Hopitaux, (1984) 60/44-45 (3137-3161).
SO
     CODEN: SHPAAI
     The definition of \ensuremath{\operatorname{migraine}} proposed by the ad hoc committee in
AB
     its classification of the different forms of headache is the most widely
     accepted. In this chapter, currently established physiopathological
     mechanisms of migraine attacks with the different stages of
     encephalic vasomotor disorders and the humoral changes which produce them
     are exposed. A description is given of the as yet incompletely understood
     constitutional anomalies that predispose to migraine; these
     include platelet function disorders currently considered as central, but
     also other factors such as hypersensitivity to dopamine or alterations.
        complied with. Ergot toxicity is usually the result of excessive dosage
     or overprolonged use. The chapter on maintenance therapy of
     migraine addresses only the most widely used drugs whose
     effectiveness has been established by controlled trials. Such drugs are
     numerous, have. . . stabilizers of vascular tone (dihydroergotamine,
     clonidine, flunarizine), substances that interfere with serotonin
     (methysergide, pizotifen, dimetotiazine, oxetorone), beta blocking agents
     (propranolol, timolol), platelet aggregation inhibitors
     (acetylsalicylic acid, dipyramidole), antidepressants (tricyclic
     antidepressants, lithium). Maintenance treatment is justified only if
     attacks recur frequently and.
     Medical Descriptors:
     *adverse drug reaction
     *artery spasm
     *drug interaction
       *migraine
     *pharmacokinetics
     *drug therapy
     peripheral vascular system
     muscle
     therapy
     human
     central nervous system
     *acebutolol
     *acetylsalicylic acid
     *alprenolol
     *aminophenazone
     *amitriptyline
     *antimigraine agent
     *atenolol
     *beta adrenergic receptor blocking agent
     *caffeine
     *clomipramine
     *clonidine
     *dexpropranolol
     *dihydroergotamine mesilate
     *dimetotiazine
     *ergotamine
     *ergotamine tartrate
     *flufenamic acid
```

```
*flunarizine
*imipramine
*lithium carbonate
*mefenamic acid
*methysergide
*metoprolol
*nadolol
*oxetorone
*oxprenolol
*phenacetin
*pindolol
*pizotifen
*practolol
*propranolol
*propyphenazone
*timolol
anticoaqulant agent
antihypertensive agent
tuberculostatic agent
cholinergic.
. . 363-24-6; (quinidine) 56-54-2; (sulfinpyrazone) 57-96-5;
(troleandomycin) 2751-09-9; (tyramine) 51-67-2, 60-19-5; (verapamil)
152-11-4, 52-53-9; (dipyridamole) 58-32-2; (oxetorone fumarate)
34522-46-8; (timolol maleate) 26921-17-5; (pizotifen maleate)
24359-22-6; (dimetotiazine mesylate) 13115-40-7
ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
85011557 EMBASE
1985011557
Migraine prevention with timolol. A double-blind
crossover study.
Stellar S.; Ahrens S.P.; Meibohm A.R.; Reines S.A.
Department of Neurosurgery, St Barnabas Medical Center, Livingston, NJ
07039, United States
Journal of the American Medical Association, (1984) 252/18
(2576-2580).
CODEN: JAMAAP
United States
Journal
        Adverse Reactions Titles
038
037
        Drug Literature Index
800
        Neurology and Neurosurgery
030
        Pharmacology
English
Migraine prevention with timolol. A double-blind
crossover study.
Journal of the American Medical Association, (1984) 252/18
(2576-2580).
CODEN: JAMAAP
One hundred seven patients (77 women and 30 men) with migraine
headache were given prophylactic treatment with timolol maleate,
20 to 30 mg/day, or matching placebo during a 20-week, double-blind
crossover study. Among the 94 patients who completed the study,
timolol was significantly better than placebo in terms of a
decrease in frequency of headaches from baseline, numbers of patients who
had a 50% reduction in headache frequency, global response, and patient
preference. Overall global response rates were 65% with timolol
compared with 40% with placebo. The severity and duration of headaches
that occurred were unchanged. Few side effects were reported with either
timolol or placebo. The study demonstrates that the \beta	ext{-blocker}
timolol is a safe and effective treatment in patients with
```

RN.

ΑN

DN

TI

ΑU

CS

SO

CY

FS

LA

ΤI

SO

ΑB

```
frequent migraine headaches.
CT
    Medical Descriptors:
    *adverse drug reaction
     *constipation
     *drug efficacy
     *fatique
     *gastrointestinal toxicity
     *insomnia
       *migraine
     *neurotoxicity
     *drug therapy
     *stomach pain
     *vertigo
    prevention
    priority journal
     large intestine
     stomach
     therapy
     intoxication
     nervous system
     oral drug administration
     human
     central nervous system
     controlled study
     major clinical study
     *timolol
     *timolol maleate
     acetylsalicylic acid
     butalbital
     caffeine
     ergotamine
     paracetamol
     placebo
     (timolol) ·26839-75-8; (timolol maleate) 26921-17-5;
RN
     (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,
     63781-77-1; (butalbital) 51005-25-5, 77-26-9; (caffeine) 30388-07-9,
     58-08-2; (ergotamine) 113-15-5, 52949-35-6; (paracetamol) 103-90-2
L11 ANSWER 10 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
ΑN
     83065958 EMBASE
     1983065958
DN
     The prophylactic effect of timolol versus propranolol and
TI
     placebo in common migraine: Beta-blockers in migraine.
ΑU
     Neurol. Dep., Ulleval Hosp., Oslo 1, Norway
CS
SO
     Cephalalgia, (1982) 2/3 (165-170).
     CODEN: CEPHDF
CY
     Norway
DТ
     Journal
             Neurology and Neurosurgery
FS
     800
             Drug Literature Index
     037
LΑ
     The prophylactic effect of timolol versus propranolol and
TΙ
     placebo in common migraine: Beta-blockers in migraine.
SO
     Cephalalgia, (1982) 2/3 (165-170).
     CODEN: CEPHDF
     A multicentre double-blind, cross-over trial was planned to evaluate the .
AΒ
     prophylactic effect of timolol in migraine. The
     effectiveness of the drug was compared to propranolol and placebo. In the
     Norwegian part of the trial described in this paper, 18 patients completed
     the study. The data suggest that timolol is equivalent in
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effectiveness to propranolol in migraine prophylaxis. Firm
conclusions should not be drawn until the results from the multicentre
trial are available.
Medical Descriptors:
*headache
  *migraine
*drug therapy
therapy
human
central nervous system
prevention
clinical article
*placebo
*propranolol
*timolol
timolol maleate
(propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6;
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(timolol) 26839-75-8; (timolol maleate) 26921-17-5

CT

RN

(FILE 'HOME' ENTERED AT 14:41:54 ON 15 DEC 2004)

FILE 'REGISTRY' ENTERED AT 14:42:04 ON 15 DEC 2004

1 S ETORICOXIB/CN L1L2

1 S TIMOLOL/CN

L3 1 S (TIMOLOL MALEATE)/CN

> FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, ...' ENTERED AT 14:43:14 ON 15 DEC 2004

L4	3	S L1 AND L3
L5	62	S L1 AND MIGRAINE
L6	15	S L5 AND PD<2003
L7	14	DUP REM L6 (1 DUPLICATE REMOVED)
T8	94	S L3 AND MIGRAINE
L9	78	S L8 AND PD<2003
L10	74	DUP REM L9 (4 DUPLICATES REMOVED)
L11	10	S L10 AND (TIMOLOL (P) MIGRAINE)

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2000:314539 CAPLUS
ΑN
     132:329940
DN
     Pharmaceutical compositions containing histaminergic agonist and COX-2
TI
     inhibitor for migraine treatment
     Simitchieva, Kremena; Reines, Scott A.; Mckinney, Errol; Sandquist, Eric
IN
     J.; Khanna, Deepak K.; Hargreaves, Richard
PA
     Merck & Co., Inc., USA
     PCT Int. Appl., 16 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
                                                                    DATE
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                                                                    19991029
     WO 2000025779
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             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
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     US 2002016348
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     US 6384034
                                20020507 /
                          B2
                                            US 2002-106845
                                                                    20020326
     US 2002177617
                                20021128
                          A1
                                19981102
PRAI US 1998-106605P
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                                19991029
     US 1999-429274
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     WO 1999-US25388
                          W
                                19991029
     US 2001-934823
                                20010822
                          А3
              THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 9
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
     Pharmaceutical compositions containing histaminergic agonist and COX-2
TI
     inhibitor for migraine treatment
     A combination of a 5HT1B/1D agonist and a cyclooxygenase-2 (COX-2)
AΒ
     selective inhibitor is useful in the treatment and/or prevention of
     migraine. The 5HT1B/1D agonist is selected from sumatriptan,
     naratriptan, zolmitriptan, eletriptan, almotriptan, and rizatriptan, and
     the COX-2 inhibitor is selected from meloxicam, MK-663
      Vioxx, RS 57067, celecoxib, and compound I. The 5HT1B/1D agonist and
     COX-2 inhibitor are administered combined in a single dosage form or as
     sep. dosage forms administered concurrently. Tablets containing 5 and 10 mg
     of rizatriptan benzoate and 10 mg Vioxx were prepared
     cyclooxygenase inhibitor histaminergic agonist tablet migraine
ST
IT
        (5-HT1B; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     5-HT agonists
        (5-HT1D; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     Antimigraine agents
         (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
```

ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

L4

IT 39391-18-9, Cyclooxygenase

=>

RL: BSU (Biological study, unclassified); BIOL (Biological study) (2, inhibitors; tablets containing histaminergic agonist and COX-2 inhibitor for migraine treatment)

TT 71125-38-7, Meloxicam 103628-46-2, Sumatriptan 121679-13-8,
Naratriptan 139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
144034-80-0, Rizatriptan 145202-66-0, Rizatriptan benzoate
154323-57-6, Almotriptan 162011-90-7, Vioxx 169590-42-5, Celecoxib
179382-91-3, RS 57067 180200-69-5 202409-33-4, MK
663

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tablets containing histaminergic agonist and COX-2 inhibitor for **migraine** treatment)

MG + CX2

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ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
    2003:260861 CAPLUS
ΑN
    138:276275
DN
    Cyclooxygenase-2 inhibitor compositions with rapid onset of therapeutic
ΤI
    Kararli, Tugrul T.; Kontny, Mark J.; Desai, Subhash; Hageman, Michael J.;
TN
    Haskell, Royal J.; Hassan, Fred; Forbes, James C.
PA
    U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 731,350.
SO
    CODEN: USXXCO
DT
    Patent
LΑ
    English
FAN.CNT 11
    PATENT NO.
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                                                                DATE
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                                          US 2001-874504
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                                          US 2002-113157
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PRAI US 1999-169856P
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    US 2000-731350
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    US 2000-31898
                              20001206
    WO 2000-US32434 W
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                             20010605
                       A1
    US 2001-874504
    MARPAT 138:276275
OS
                              DATE
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                                                                DATE
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                                          US 2001-874504
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                        A1
                              20030403
                                                                20010605
PI
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IT
    Headache
        (migraine; cyclooxygenase-2 inhibitor compns. with rapid
       onset of therapeutic effect)
    58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological
ΙT
    studies 69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine
    162011-90-7, Rofecoxib 169590-41-4, Deracoxib 181695-72-7, Valdecoxib
    202409-33-4 212126-32-4 215123-80-1
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (cyclooxygenase-2 inhibitor compns. with rapid onset of therapeutic
       effect)
    ANSWER 2 OF 14 USPATFULL on STN
L7
                                                      DUPLICATE 1
      2002:27500 USPATFULL
AN
      Method of treating migraines and pharmaceutical compositions
TI
IN
      Simitchieva, Kremena, Basking Ridge, NJ, UNITED STATES
      Reines, Scott A., New Hope, PA, UNITED STATES
      Mckinney, Errol, Doylestown, PA, UNITED STATES
      Sandquist, Eric J., Doylestown, PA, UNITED STATES
      Khannna, Deepak K., Furlong, PA, UNITED STATES
      Hargreaves, Richard, Terlings Park, UNITED KINGDOM
PA
      Merck & Co. Inc. (U.S. corporation)
РΤ
      US 2002016348
                        Α1
                             20020207
                                                                  <--
      US 6384034
                         B2
                             20020507
                        Al
                             20010822 (9)
      US 2001-934823
AΤ
      Continuation of Ser. No. US 1999-429274, filed on 29 Oct 1999, PENDING
RLI
      US 1998-106605P 19981102 (60)
PRAI
DΤ
      Utility
FS
      APPLICATION
LREP
      RICHARD C. BILLUPS, Patent Department, Merck & Co. Inc., P.O. Box 2000,
      Rahway, NJ, 07065-0907
CLMN
      Number of Claims: 10
\mathsf{ECL}
      Exemplary Claim: 1
DRWN
      No Drawings
LN.CNT 331
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FAN.CNT 1

PATENT NO.

KIND

DATE

APPLICATION NO.

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WO 2002-US21069
    WO 2002100352
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                                20021219
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                                20030327
    WO 2002100352
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    US 2004204341
                         A1
                         Ρ
                                20010612
PRAI US 2001-297672P
                                20020607
    WO 2002-US21069,
                         W
     Preparation of piperidinecarboxylates and related compounds as NMDA NR2B
TI
     receptor antagonists for the treatment or prevention of migraine
     WO 2002100352 A2 20021219
PΙ
                                          APPLICATION NO.
                                                                  DATE
                       KIND DATE
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                        A2
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             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
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             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                        A1 20041014 US 2003-479923
                                                                   20031205
     US 2004204341
     piperidinecarboxylate prepn NR2B receptor antagonist; migraine
ST
     treatment piperidinecarboxylate prepn
ΙT
     5-HT agonists
        (5-HT1B, coadministration; preparation of piperidinecarboxylates and related
        compds. as NR2B receptor antagonists for the treatment or prevention of
        migraine)
IT
     5-HT agonists
        (5-HT1D, coadministration; preparation of piperidinecarboxylates and related
        compds. as NR2B receptor antagonists for the treatment or prevention of
        migraine)
     Calcitonin gene-related peptide receptors
TT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (ligands, coadministration; preparation of piperidinecarboxylates and
        related compds. as NR2B receptor antagonists for the treatment or
        prevention of migraine)
IT
     Headache
        (migraine, treatment; preparation of piperidinecarboxylates and
        related compds. as NR2B receptor antagonists for the treatment or
        prevention of migraine)
ΙT
     Antimigraine agents
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
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20020607 <--

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antagonists for the treatment or prevention of migraine)
     Glutamate receptors
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
        antagonists for the treatment or prevention of migraine)
                               121679-13-8, Naratriptan
                                                            139264-17-8,
ΙT
     103628-46-2, Sumatriptan
                                              144034-80-0, Rizatriptan
     Zolmitriptan
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                 169590-42-5, Celecoxib
                                          180200-68-4, JTE522
                                          198470-84-7, Parecoxib
                  197438-48-5, BMS347070
     Valdecoxib
     202409-33-4, Etoricoxib
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                            346670-87-9, CS 502 (pharmaceutical)
     266320-83-6, ABT 963
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (coadministration; preparation of piperidinecarboxylates and related compds.
        as NR2B receptor antagonists for the treatment or prevention of
        migraine)
IT
     455265-37-9P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
        (preparation of piperidinecarboxylates and related compds. as NR2B receptor
        antagonists for the treatment or prevention of migraine)
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     366022-97-1P
                    455265-19-7P, Benzyl 4-[(4-pyridinylamino)methyl]-1-
                             455265-20-0P, Benzyl 4-[[(3-
     piperidinecarboxylate
     pyridinyl)amino]methyl]-1-piperidinecarboxylate
                                                        455265-21-1P, Benzyl
     4-[(3-isoxazolylamino)methyl]-1-piperidinecarboxylate
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                    455265-25-5P, 4-[(3-Methylpyridin-4-
     455265-24-4P
     ylamino)methyl]piperidine-1-carboxylic acid benzyl ester
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     Benzyl 4-[[(4-methyl-2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
     455265-28-8P, Benzyl 4-[(1,3,4-thiadiazol-2-ylamino)methyl]-1-
     piperidinecarboxylate
                            455265-30-2P
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     4-[[(2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
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     Benzyl 4-[[(4-ethyl-2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
     455265-34-6P, Benzyl 4-[[(1-oxido-4-pyridinyl)amino]methyl]-1-
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     piperidinecarboxylate
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                                                    455290-06-9P, Benzyl
     4-[[(5-methyl-2-pyridinyl)amino]methyl]-1-piperidinecarboxylate
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                                               478552-68-0P, Benzyl
 4-[[(1-methyl-1H-imidazol-2-yl)amino]methyl]-1-piperidinecarboxylate
 478552-69-1P, 4-(Quinolin-2-ylaminomethyl)piperidine-1-carboxylic acid
 benzyl ester
                478552-71-5P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
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                           55-22-1, Isonicotinic acid, reactions
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 51-21-8, 5-Fluorouracil
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 6-Chloropurine
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 acid, reactions
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 Benzaldehyde, reactions
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 Benzenepropanal
                   108-00-9, N,N-Dimethylethylenediamine
                                                             122 - 59 - 8,
 Phenoxyacetic acid
                      123-38-6, Propionaldehyde, reactions
                          155-10-2, 2-Chloro-5-fluoropyrimidin-4-ylamine
 3,6-Dichloropyridazine
                             456-47-3, 3-Fluorobenzyl alcohol
 372-48-5, 2-Fluoropyridine
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 3-Aminopyridine
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 isothiocyanate
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471248-78-9P

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1450-93-7, 2-Aminoimidazole hemisulfate
                                         1603-40-3, 2-Amino-3-
                1603-41-4, 2-Amino-5-methylpyridine 1681-15-8
methylpyridine
1722-12-9, 2-Chloropyrimidine
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2,4-Dichloro-5-methylpyrimidine 1875-88-3, 2-(4-Chlorophenyl)ethanol
1990-90-5, 4-Amino-3-methylpyridine
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2-(2-Fluorophenyl)ethanol
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3-(2-Aminomethyl)pyridine
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d]pyrimidine
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2,4-Dichloropyrimidine 4005-51-0, 2-Amino-1,3,4-thiadiazole
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1H-Benzimidazol-4-ylamine
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2,3-Dichloropyrazine
2,4-Dichloro-6-methylpyrimidine 5440-17-5
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1-Benzyl-4-hydroxypiperidine-4-carbonitrile
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4-Methylthiopteridine
7144-05-0, 4-Aminomethylpiperidine 7461-50-9, 2-Chloropyrimidin-4-
         7589-27-7, 2-(4-Fluorophenyl)ethanol
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1-[(Benzyloxy)carbonyl]-4-piperidinecarboxylic acid
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Potassium thioacetate 13036-57-2, 2-Chloro-4-methylpyrimidine
            13534-90-2, 3,4-Dibromopyridine 17012-21-4
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13139-17-8
4-Bromopyridine hydrochloride 20781-20-8, 2,4-Dimethoxybenzylamine
20928-46-5 22282-75-3, 3-Fluoro-4-iodopyridine
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2-Chloro-5-methylpyrimidine
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acid amide
Cyclopropylmagnesium bromide 24225-89-6, 1,4-Dibenzyl-2-
chloromethylpiperazine 27048-04-0, 6-Chloro-3-nitropyridin-2-ylamine
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Phenylcyclopropanecarboxaldehyde
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oxopiperidine-4-carboxylate 49844-90-8, 4-Chloro-2-methylthiopyrimidine
51171-02-9, 3-Bromopyrazine-2-carboxylic acid methyl ester
Ethyl 4-iodobenzoate 52147-97-4 52334-53-9, 4-Aminopyridin-3-ol
52763-21-0, Ethyl N-benzyl-3-oxopiperidine-4-carboxylate hydrochloride
59870-43-8, 2-Chloroquinazolin-4-ylamine
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N-[(4-Chlorobenzyloxy)carbonyloxy]succinimide
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Thiophen-3-ylmethanol 79521-61-2 110105-91-4, N-(4-Piperidinylmethyl)-
4-pyridinamine 110859-47-7 128595-01-7 138163-08-3, Benzyl
4-formyl-1-piperidinecarboxylate 148148-48-5
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2-tert-Butoxycarbonylaminopyrimidine-5-carboxylic acid
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4-Methylbenzyl 4-(aminomethyl)-1-piperidinecarboxylate
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carboxylate
1H-Pyrazole-4-carboxylic acid (piperidin-4-ylmethyl) amide
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2-(Diethyloxymethyl)isonicotinic acid ethyl ester 23804-68-4P,
4-Aminomethyl-1-benzylpiperidin-4-ol 35391-85-6P, 4-Cyclopropylbenzoic
acid ethyl ester 39478-61-0P, 1-Benzyl-4-hydroxymethylpiperidin-3-ol
41438-38-4P, 2,4-Pyridinedicarboxylic acid diethyl ester
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2-Chloro-5-fluoropyrimidine 85151-16-2P
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4-[(4-pyridinylamino)carbonyl]-1-piperidinecarboxylate
115687-29-1P, 1-Benzylpyrrolidine-3-carboxylic acid amide
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carboxylic acid tert-butyl ester 155456-33-0P 157023-34-2P, Benzyl

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4-(aminomethyl)piperidine-1-carboxylate
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    4-Acetylpiperidine-1-carboxylic acid benzyl ester 172348-56-0P
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                    454678-87-6P, (4-Cyclopropylphenyl)methanol
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    455267-05-7P, Benzyl 4-[[(1-oxido-4-pyridinyl)amino]carbonyl]-1-
                                            455267-07-9P, (cis)-3-Hydroxy-4-
    piperidinecarboxylate
                            455267-06-8P
     [(2,3,5,6-tetrachloropyridin-4-ylamino)methyl]piperidine-1-carboxylic acid
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    benzyl ester
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     2-(Diethyloxymethyl)isonicotinic acid 471254-07-6P
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                    471254-12-3P, 3-Hydroxy-4-hydroxymethylpiperidine-1-
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     carboxylic acid benzyl ester 471254-13-4P, 4-Hydroxy-N-pyridin-3-
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    ylmethylbenzamide
     471254-16-7P, N-(1,4-Dibenzylpiperazin-2-ylmethyl)-4-hydroxybenzamide
     471254-17-8P, 4-Hydroxy-N-piperazin-2-ylmethylbenzamide
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    N-(4-Benzylmorpholin-2-ylmethyl)-4-hydroxybenzamide
     478552-72-6P, (trans)-3-Hydroxy-4-hydroxymethylpiperidine-1-carboxylic
     acid benzyl ester
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     329900-75-6, Cyclooxygenase-2
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    ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
     2002:868732 CAPLUS
     137:363084
     Use of cyclooxygenase inhibitors for treating migraines
    Allen, Christopher; Stone, Phyllis; Harper, Sean
    Merck & Co., Inc., USA
     PCT Int. Appl., 15 pp.
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     cyclooxygenase inhibitor migraine treatment'
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     Headache
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     50-33-9, Phenylbutazone, biological studies
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     50-78-2, Aspirin 52-53-9, Verapamil 53-86-1, Indomethacin 54-21-7,
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     Ergocryptine 511-12-6, Dihydroergotamine 525-66-6, Propranolol
     530-78-9, Flufenamic acid 552-94-3, Salsalate 561-94-4, Ergosine
     599-79-1, Sulfasalazine 644-62-2, Meclofenamic acid 2854-38-8, Ergostine 8067-24-1, Ergoloid mesylates 13539-59-8, Apazone
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     Bromocriptine
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     59804-37-4, Tenoxicam 70374-39-9, Lornoxicam 71125-38-7, Meloxicam
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     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
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        (use of cyclooxygenase inhibitors for treating migraines)
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     ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
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     2002:813958 CAPLUS
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     Oral pharmaceutical compositions comprising a low-water-soluble drug, a
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     solvent, a fatty acid and an organic amine
     Ṣao, Ping; Karim, Aziz; Hassan, Fred; Forbes, James C.
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     PCT Int. Appl., 67 pp.
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PRAI US 2001-284381P
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                          Ρ
                                 20011004
     WO 2002-US11689
                          W
                                 20020412
OS
     MARPAT 137:316089
RE.CNT
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
     WO 2002083177 A1 20021024
PΙ
                                             APPLICATION NO.
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                                 20031210
                                                                      20031016
IT
     Headache
        (migraine; oral pharmaceutical compns. comprising
        low-water-soluble drug and solvent and fatty acid and organic amine)
IT
     57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid,
     biological studies 60-33-3, Linoleic acid, biological studies
     69-89-6D, Xanthine, alkyl derivs. 77-86-1, Tromethamine
     Triethanolamine, biological studies 108-01-0, Dimethylaminoethanol
     111-42-2, Diethanolamine, biological studies 112-79-8, Elaidic acid
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112-80-1, Oleic acid, biological studies 124-07-2, Octanoic acid,

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Pharmacia Corporation, USA

141-43-5, Monoethanolamine, biological studies biological studies 142-62-1, Caproic acid, biological studies 143-07-7, Lauric acid, biological studies 334-48-5, Capric acid 463-40-1, Linolenic acid 506-30-9, Eicosanoic acid 544-63-8, Myristic acid, biological studies 13296-76-9, Eleostearic acid 25322-68-3, Polyethylene glycol 32839-30-8, Eicosapentaenoic acid 162011-90-7, Rofecoxib 32839-18-2 169590-41-4, Deracoxib 181695-72-7, Valdecoxib 202409-33-4, 212126-32-4 215123-80-1 Etoricoxib 266320-83-6 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oral pharmaceutical compns. comprising low-water-soluble drug and solvent and fatty acid and organic amine) ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2002:555346 CAPLUS 137:114529 Pharmaceutical composition having reduced tendency for drug crystallization Gao, Ping; Hageman, Michael J.; Morozowich, Walter; Dalga, Robert J.; Stefanski, Kevin J.; Huang, Tiehua; Karim, Aziz; Hassan, Fred; Forbes, James C. Pharmacia Corporation, USA PCT Int. Appl., 65 pp. CODEN: PIXXD2 Patent English FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ______ ____ _____ ______ _____ WO 2002056878 A2 20020725 WO 2002-US971 20020115 <--WO 2002056878 А3 20021219 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2002-47902 US 2002156124 Α1 20021024 20020114 <--CA 2434338 AA20020725 CA 2002-2434338 20020115 <--US 2003045563 A1 20030306 US 2002-47222 20020115 EP 1365812 A2 20031203 EP 2002-709027 20020115 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR BR 2002006580 Α 20031216 BR 2002-6580 20020115 JP 2004520359 Т2 20040708 JP 2002-557386 ... 20020115 NO 2003003244 Α 20030917 NO 2003-3244 20030717 PRAI US 2001-262555P Ρ 20010118 US 2001-284608P Ρ 20010417 WO 2002-US971 W 20020115 MARPAT 137:114529 WO 2002056878 A2 20020725 APPLICATION NO. PATENT NO. KIND DATE DATE _____ _____ ____ ______ WO 2002056878 A2 20020725 WO 2002-US971 20020115 <--WO 2002056878 A3 20021219 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ. TM
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                                                                     20020114 <--
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                                             US 2002-47222
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                          A1
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     BR 2002006580
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     JP 2004520359
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                                 20040708
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     NO 2003003244
                          Α
                                 20030917
                                             NO 2003-3244
                                                                     20030717
ΙT
     Headache
        (migraine; pharmaceutical composition having reduced tendency for
        drug crystallization)
IT
     56-81-5, Glycerin, biological studies 58-08-2, Caffeine, biological
               58-55-9, Theophylline, biological studies
                                                            69-89-6D, Xanthine,
                     83-67-0, Theobromine 9003-39-8, PVP
                                                              9004-32-4,
     alkyl derivs.
     Carboxymethyl cellulose sodium salt
                                            9004-34-6D, Cellulose, derivs.
     9004-54-0, Dextran, biological studies
                                               9004-57-3, Ethyl cellulose
     9004-64-2, Hydroxypropyl cellulose 9004-65-3, HPMC
                                                             9004-67-5, Methyl
                25322-68-3, Polyethylene glycol 162011-90-7, Rofecoxib
                              181695-72-7, Valdecoxib 202409-33-4,
     169590-41-4, Deracoxib
                  212126-32-4
                                215123-80-1
                                               266320-83-6
     Etoricoxib
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition having reduced tendency for drug
crystallization)
     ANSWER 7 OF 14 USPATFULL on STN
L7
AN
       2002:315130 USPATFULL
ΤI
       Method of treating migraines and pharmaceutical compositions
       Simitchieva, Kremena, Basking Ridge, NJ, UNITED STATES
İΝ
       Reines, Scott A., New Hope, PA, UNITED STATES
       McKinney, Errol, Doylestown, PA, UNITED STATES
       Sandquist, Eric J., Doylestown, PA, UNITED STATES
       Khannna, Deepak K., Furlong, PA, UNITED STATES
       Hargreaves, Richard, Terlings Park, UNITED KINGDOM
PA
       Merck & Co., Inc. (U.S. corporation)
PΙ
       US 2002177617
                          A1
                               20021128
       US 2002-106845
                                20020326 (10)
ΑI
                          Α1
RLT
       Division of Ser. No. US 2001-934823, filed on 22 Aug 2001, GRANTED, Pat.
       No. US 6384034 Continuation of Ser. No. US 1999-429274, filed on 29 Oct
       1999, ABANDONED
PRAI
       US 1998-106605P
                           19981102 (60)
DT
       Utility
FS
       APPLICATION
       MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
LREP
CLMN
       Number of Claims: 10
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI
       US 2002177617
                          A1
                                20021128
       A combination of a 5HT.sub.1B/1D agonist and a COX-2 selective inhibitor
AΒ
       is useful in the treatment and or prevention of migraine.
SUMM
       . . . has been known for some time that sumatriptan, which causes
       constriction of cranial blood vessels, is an effective treatment for
       migraine (see, for example, Doenicke et al., Lancet, 1988, Vol.
       1, 1309-11; and Feniuk & Humphrey, Drug Development Research, 1992, 26,.
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. . . within the trigeminal nucleus caudalis. It is believed that one
       or more of these three mechanisms is involved in the anti-
       migraine action of 5-HT.sub.1B/1D receptor agonists such as
       rizatriptan.
       . . . \mbox{\it method} of treating or preventing \mbox{\it migraines} in a \mbox{\it mammalian}
SUMM
       patient in need thereof, which comprises administering to said patient
       an anti-migraine effective amount of a combination of a COX-2
       selective inhibitor and a 5-HT.sub.1B/1D receptor agonist.
SUMM
       [0010] One embodiment of the present invention is a method of treating
       or preventing migraine with an anti-migraine
       effective amount of a combination of a 5HT.sub.1B/1D agonist and a COX-2
       selective inhibitor. Another embodiment of the invention is.
       [0015] In one aspect of the invention, a method of treating or
SUMM
       preventing migraine is disclosed in a mammalian patient in
       need of such treatment, which comprises administering to the patient a
       COX-2 selective.
       [0024] An anti-migraine effective amount of the combination is
SUMM
       that amount that will relieve the subject being treated of the symptoms
       of the migraine attack and the specific dose level and
       frequency of dosage may vary and will depend upon a variety of factors.
SUMM
       [0025] For the treatment of a migraine attack, the active
       ingredients, separately or in combination, may be administered orally,
       topically, parenterally, by inhalation, spray, rectally or
       intravaginally.
CLM
       What is claimed is:
       1. A method of treating or preventing migraine in a mammalian
       patient in need of such treatment, which comprises administering to the
       patient a COX-2 selective inhibiting compound.
IT
      71125-38-7, Meloxicam 103628-46-2, Sumatriptan
                                                          121679-13-8,
                    139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
      Naratriptan
      144034-80-0, Rizatriptan
                                 145202-66-0, Rizatriptan benzoate
                                162011-90-7, Vioxx 169590-42-5, Celecoxib
      154323-57-6, Almotriptan
      179382-91-3, RS 57067
                            180200-69-5 202409-33-4, MK 663
        (tablets containing histaminergic agonist and COX-2 inhibitor for migraine
        treatment)
     ANSWER 8 OF 14 USPATFULL on STN
Ь7
       2002:221058 USPATFULL
AN
ΤI
       Oral fast-melt formulation of a cyclooxygenase-2 inhibitor
IN
       Le, Trang T., Mundelein, IL, UNITED STATES
       Kararli, Tugrul T., Skokie, IL, UNITED STATES
       Kontny, Mark J., Libertyville, IL, UNITED STATES
       Sastry, Srikonda V., Sunnyvale, CA, UNITED STATES
       Nyshadham, Janaki R., Fremont, CA, UNITED STATES
       Pagliero, Arthur J., JR., Vacaville, CA, UNITED STATES
PI
                               20020829
       US 2002119193
                          A1
                                                                     <---
       US 2001-932494
                          Α1
                               20010817 (9)
ΑI
       US 2000-226349P
                           20000818 (60)
PRAI
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       Utility
FS
       APPLICATION
LREP
       Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh
       Boulevard - 04B, St. Louis, MO, 63167
CLMN
       Number of Claims: 89
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1634
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI
       US 2002119193
                          Α1
                               20020829
SUMM
       [0061] Such compositions are useful in treating inflammation in such
       diseases as migraine headaches, periarteritis nodosa,
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SUMM

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thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic
       fever, type I diabetes, neuromuscular junction disease including
       myasthenia gravis,.
       [0074] For pain management generally and specifically for treatment and
SUMM
       prevention of headache and migraine, such compositions of the
       invention can be used to provide a daily dosage of celecoxib of about 50
       mg to. .
SUMM
       [0083] In an embodiment of the invention, particularly where the
       cyclooxygenase-2 mediated condition is headache or migraine,
       the present selective cyclooxygenase-2 inhibitory drug composition is
       administered in combination therapy with a vasomodulator, preferably a
       xanthine derivative having.
SUMM
       . . . vasomodulator or alkylxanthine are selected to be
       therapeutically and/or prophylactically effective for relief of pain
       associated with the headache or migraine. Suitable dosage
       amounts will depend on the particular selective cyclooxygenase-2
       inhibitory drug and the particular vasomodulator or alkylxanthine
       selected. For.
      162011-90-7, Rofecoxib
                               169590-41-4, Deracoxib
                                                        169590-42-5, Celecoxib
TΤ
      181695-72-7, Valdecoxib 202409-33-4, Etoricoxib
                                                        212126-32-4
      215123-80-1
                    266320-83-6
        (oral fast-melt formulation of cyclooxygenase-2 inhibitor)
     ANSWER 9 OF 14 USPATFULL on STN
L7
       2002:199141 USPATFULL
ΑN
       Rapid-onset formulation of a selective cyclooxygenase-2 inhibitor
TI
ΙN
       Hariharan, Madhusudan, Evanston, IL, UNITED STATES
       Kararli, Tugrul T., Skokie, IL, UNITED STATES
       Hassan, Fred, Peapack, NJ, UNITED STATES
       Forbes, James C., Glenview, IL, UNITED STATES
                               20020808
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PΙ
       US 2002107250
                         A1
       US 2001-836905
                         Α1
                               20010417 (9)
ΑI
       US 2000-197746P
                           20000418 (60)
PRAI
       Utility
DT
       APPLICATION .
FS
       Pharmacia Corporation, P.O. Box 5110, Chicago, IL, 60680-5110
LREP
       Number of Claims: 38
CLMN
ECL
       Exemplary Claim: 1
       2 Drawing Page(s)
DRWN
LN.CNT 1552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PΙ
       US 2002107250
                         A1
                               20020808
AB
         . . and is useful in treatment of cyclooxygenase-2 mediated
       conditions and disorders, particularly pain. For relief of pain in
       headache or migraine, the composition can optionally be
       administered together with a vasodilator.
SUMM
         . . disclose compositions comprising a selective COX-2 inhibitory
       drug, a 5HT.sub.1 receptor agonist and caffeine, said to be useful for
       treating migraine.
       . . . immediate therapeutic effect than standard dosage forms. For
SUMM
       example, in the treatment of acute pain, for example in headache or
       migraine, rapid-onset dosage forms would be useful to provide
       fast pain relief.
SUMM
          . . important advance in the art to provide an effective method of
       treatment of acute pain, for example in headache or migraine,
       using such a formulation.
SUMM
       . . . selective COX-2 inhibitory drug composition of the invention.
       In another embodiment, a method of treatment and/or prevention of
       headache or migraine is provided comprising orally
       administering, to a subject in need of such treatment or prevention, an
       aminosulfonyl-comprising selective COX-2 inhibitory.
       [0212] Such compositions are useful in treating inflammation in such
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diseases as migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic fever, type I diabetes, neuromuscular junction disease including myasthenia gravis,. . .

- DETD . . . for treatment of acute COX-2 mediated disorders, especially for relief of pain, for example in headache, including sinus headache and migraine.
- DETD . . . surgery pain, post-general surgery pain, post-orthopedic surgery pain, and acute flares of osteoarthritis), for prevention and treatment of headache and migraine, for treatment of Alzheimer's disease, and for colon cancer chemoprevention.
- DETD [0226] For pain management generally and specifically for treatment and prevention of headache and migraine, compositions of the invention can be used to provide a daily dose of celecoxib of about 50 mg to about. . .
- DETD [0234] In an embodiment of the invention, particularly where the COX-2 mediated condition is headache or migraine, the present selective COX-2 inhibitory drug composition is administered in combination therapy with a vasomodulator, preferably a xanthine derivative having. . .
- DETD . . . vasomodulator or alkylxanthine are selected to be therapeutically and/or prophylactically effective for relief of pain associated with the headache or migraine. Suitable dosage amounts will depend on the particular selective COX-2 inhibitory drug and the particular vasomodulator or alkylxanthine selected. For. . CLM What is claimed is:
 - . . cyclooxygenase-2 inhibitory drug and the vasomodulator are present in total and relative amounts effective to relieve pain in headache or migraine.
 - . inhibitory drug and the alkylxanthine compound are present in total and relative amounts effective to relieve pain in headache or migraine.
 - 33. The method of claim 32 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject a vasomodulator, the selective cyclooxygenase-2 inhibitory drug and the vasomodulator being administered in total and relative amounts effective to relieve pain in the headache or migraine.
 - 35. The method of claim 32 wherein the subject suffers from headache or migraine and wherein there is further orally administered to the subject an alkylxanthine compound, the selective cyclooxygenase-2 inhibitory drug and the alkylxanthine compound being administered in total and relative amounts effective to relieve pain in the headache or migraine.
- ΙT 58-08-2, Caffein, biological studies 58-55-9, Theophylline, biological 69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine 110-71-4, Ethylene glycol dimethyl ether 110-80-5, Ethylene glycol monoethyl ether 111-76-2, Ethylene glycol monobutyl ether Diethylene glycol monomethyl ether 111-90-0, Diethylene glycol monoethyl ether 111-96-6, Diethylene glycol dimethyl ether Diethylene glycol diethyl ether 112-48-1, Ethylene glycol dibutyl ether 112-49-2, Triethylene glycol dimethyl ether 112-50-5, Triethylene glycol monoethyl ether 112-73-2, Diethylene glycol dibutyl ether 122-99-6, Ethylene glycol monophenyl ether 124-07-2D, Caprylic acid, 143-22-6, Triethylene glycol monobutyl ether glycerides 143-24-8, Tetraethylene glycol dimethyl ether 334-48-5D, Capric acid, glycerides 622-08-2, Ethylene glycol monobenzyl ether 629-14-1, Ethylene glycol diethyl ether 764-99-8, Diethylene glycol divinyl ether 18912-80-6, Diethylene glycol monoisobutyl ether 37321-62-3, Propylene glycol

68958-64-5, Polyoxyethylene glyceryl trioleate 63980-40-5 162011-90-7, Rofecoxib 169590-41-4, Deracoxib 156259-68-6, Capmul mcm 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 202409-33-4, 215123-80-1 247074-38-0 266320-83-6 212126-32-4 (rapid-onset formulation of selective cyclooxygenase-2 inhibitors) ANSWER 10 OF 14 USPATFULL on STN 2002:149172 USPATFULL Selective cyclooxygenase-2 inhibitors and vasomodulator compounds for generalized pain and headache pain Hassan, Fred, Peapack, NJ, UNITED STATES Forbes, James C., Skokie, IL, UNITED STATES US 2002077328 A1 20020620 <--US 2001-905292 **A**1 20010713 (9) 20010606 (60) US 2001-296196P US 2001-284248P 20010417 (60) US 2000-218101P 20000713 (60) Utility APPLICATION SENNIGER POWERS LEAVITT AND ROEDEL, ONE METROPOLITAN SQUARE, 16TH FLOOR, ST LOUIS, MO, 63102 Number of Claims: 125 Exemplary Claim: 1 10 Drawing Page(s) LN.CNT 4527 CAS INDEXING IS AVAILABLE FOR THIS PATENT. US 2002077328 A1 20020620 . . disclose compositions comprising a selective COX-2 inhibitory drug, a 5HT.sub.1 receptor agonist and caffeine, said to be useful for treating migraine. . . immediate therapeutic effect than standard dosage forms. For example, in the treatment of acute pain, for example in headache or migraine, rapid-onset dosage forms would be useful to provide fast pain relief. . . . mechanisms giving rise to pain, especially headache pain. Under the vasogenic theory, intracranial vasoconstriction was responsible for the symptoms of migraine aura and headache resulted from a rebound dilation and distention of cranial vessels and activation of perivascular nociceptive axons. However, under the alternate nerogenic theory, the brain generates the migraine and susceptibility to migraine attacks reflects thresholds intrinsic to the individual's brain. Thus, vascular changes occurring during migraine are the result and not the cause of the attack. Even considering the alternate theories of migraine, vascular changes are implicated as an important event during the headache. Thus, using a vasomodulator to affect vascular changes in. . . . cyclooxygenase-2 inhibitor compound a vasomodulator, the pain can be generalized pain or headache pain. The headache pain can be from migraine headache pain, cluster headache pain, chronic daily headache pain, substance-induced headache pain, tension or stress related headache pain, sinus headache. . . arteritis, or headache pain resulting from lumbar puncture. A very important preference for this invention is pain which results from migraine pain. Another important preference in the present invention is pain resulting from a cluster headache. Another preferred source of pain. What is claimed is: 11. The combination according claim 10 wherein the headache pain is selected from the group consisting of migraine headache pain, cluster headache pain, chronic headache pain, substance-induced headache

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ΑN

TI

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DT

FS : LREP

CLMN ECL

DRWN

PΙ

SUMM

SUMM

DETD

DETD

CLM

PRAI

111. The method according to claim 106 wherein the pain is selected from

pain, tension or stress related headache pain, sinus headache pain,.

the group consisting of migraine headache pain, cluster headache pain, chronic headache pain, substance-induced headache pain, tension or stress related headache pain, sinus headache pain,. . 162011-90-7, Rofecoxib IT254-04-6D, Benzopyran, derivs. 169590-42-5, Celecoxib 181695-72-7, Valdecoxib Deracoxib 198470-84-7, Parecoxib **202409-33-4**, Etoricoxib 212126-32-4 266320-83-6 (cyclooxygenase 2 inhibitors for treatment and prevention of ocular COX-2-mediated disorders) L7 ANSWER 11 OF 14 USPATFULL on STN AN 2002:140876 USPATFULL TΙ Rapidly disintegrating oral formulation of a cyclooxygenase-2 inhibitor Kararli, Tugrul T., Skokie, IL, UNITED STATES IN Kontny, Mark J., Libertyville, IL, UNITED STATES Le, Trang T., Mundelein, IL, UNITED STATES PΙ US 2002071857 A120020613 <--20010817 (9) ΑI US 2001-932537 Α1 PRAI US 2000-226487P 20000818 (60) DTUtility FS APPLICATION LREP Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh Boulevard - 04B, St. Louis, MO, 63167 Number of Claims: 48 CLMN ECL Exemplary Claim: 1 DRWN No Drawings LN.CNT 1452 CAS INDEXING IS AVAILABLE FOR THIS PATENT. US 2002071857 A1 20020613 DETD [0089] Such compositions are useful in treating inflammation in such diseases as migraine headaches, periarteritis nodosa, thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic fever, type I diabetes, neuromuscular junction disease including myasthenia gravis,. [0102] For pain management generally and specifically for treatment and DETD prevention of headache and migraine, such compositions of the invention can be used to provide a daily dosage of celecoxib of about 50 mg to. DETD [0110] In an embodiment of the invention, particularly where the cyclooxygenase-2 mediated condition is headache or migraine, the present selective cyclooxygenase-2 inhibitory drug composition is administered in combination therapy with a vasomodulator, preferably a xanthine derivative having. DETD . . . vasomodulator or alkylxanthine are selected to be therapeutically and/or prophylactically effective for relief of pain associated with the headache or migraine. Suitable dosage amounts will depend on the particular selective cyclooxygenase-2 inhibitory drug and the particular vasomodulator or alkylxanthine selected. For. IT 50-70-4, Sorbitol, biological studies 50-99-7, Glucose, biological 57-27-2, Morphine, biological studies 57-42-1, Meperidine studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, 69-79-4, Maltose 76-57-3, Codeine 87-99-0, Xylitol Mannitol 149-32-6, Erythritol 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs. 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 162011-90-7, Rofecoxib 169590-41-4, 169590-42-5, Celecoxib 181695-72-7, Valdecoxib **202409-33-4,** Etoricoxib 212126-32-4 215123-80-1 266320-83-6 (rapidly disintegrating oral formulation of cyclooxygenase-2 inhibitor)

L7 ANSWER 12 OF 14 USPATFULL on STN AN 2002:92708 USPATFULL

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Kararli, Tugrul T., Skokie, IL, UNITED STATES
IN
       Kontny, Mark J., Libertyville, IL, UNITED STATES
       Le, Trang T., Mundelein, IL, UNITED STATES
PΙ
       US 2000-226347P 20000819 (9)
       US 2002049233 A1 20020425
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ΑТ
PRAI
דת
       Utility
       APPLICATION
FS
LREP
       Pharmacia Corporation, Corporate Patent Dept., 800 N. Lindbergh
       Boulevard - 04B, St. Louis, MO, 63167
CLMN
       Number of Claims: 39
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1131
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       US 2002049233 A1 20020425
PΤ
DETD
       [0049] Such compositions are useful in treating inflammation in such
       diseases as migraine headaches, periarteritis nodosa,
       thyroiditis, aplastic anemia, Hodgkin's disease, sclerodoma, rheumatic
       fever, type I diabetes, neuromuscular junction disease including
       myasthenia gravis,. . .
DETD
       [0062] For pain management generally and specifically for treatment and
       prevention of headache and migraine, such compositions of the
       invention can be used to provide a daily dosage of celecoxib of about 50
DETD
       [0069] In an embodiment of the invention, particularly where the
       cyclooxygenase-2 mediated condition is headache or migraine,
       the present selective cyclooxygenase-2 inhibitory drug composition is
       administered in combination therapy with a vasomodulator, preferably a
       xanthine derivative having.
       . . . vasomodulator or alkylxanthine are selected to be
DETD
       therapeutically and/or prophylactically effective for relief of pain
       associated with the headache or migraine. Suitable dosage
       amounts will depend on the particular selective cyclooxygenase-2
       inhibitory drug and the particular vasomodulator or alkylxanthine
       selected. For.
IT
      50-70-4, Sorbitol, biological studies 57-27-2, Morphine, biological
      studies 57-42-1, Meperidine 57-50-1, Sucrose, biological studies
      57-55-6D, Propylene glycol, esters with fatty acids 63-42-3, Lactose
      69-65-8, Mannitol 69-79-4, Maltose 76-57-3, Codeine 87-99-0, Xylitol 151-21-3, Sodium lauryl sulfate, biological studies 577-11-7,
      Dioctyl sodium sulfosuccinate 585-88-6, Maltitol 7631-86-9, Silica, biological studies 25301-02-4, Tyloxapol 25322-68-3D, Polyethylene
      glycol, derivs. 106392-12-5, Poloxamer 162011-90-7, Rofecoxib
      169590-41-4, Deracoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib 202409-33-4, Etoricoxib 212126-32-4 215123-80-1 266320-83-6
        (oral fast-melt formulation of cyclooxygenase-2 inhibitor)
L7
     ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
     2001:780682 CAPLUS
ΑN
DN
     135:335155
TI
     Rapid-onset formulation of a selective cyclooxygenase-2 inhibitors
ΙN
     Hariharan, Madhusudan; Kararli, Tugrul T.; Hassan, Fred; Forbes, James C.
PA
     Pharmacia Corporation, USA
SO
     PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DΤ
     Patent
LΑ
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
                                                                       DATE
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Oral fast-melt dosage form of a cyclooxygenase-2 inhibitor

TΙ

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    WO 2001078724
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PRAI US 2000-197746P
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    MARPAT 135:335155
OS
RE.CNT
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             ALL CITATIONS AVAILABLE IN THE RE FORMAT
    WO 2001078724 A1 20011025
PΙ
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                        KIND
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                                                                   DATE
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     JP 2004500427
                         Т2
                                                                   20010417
    An orally deliverable pharmaceutical composition is provided comprising a
AΒ
     selective cyclooxygenase-2 inhibitory drugs of low water solubility, for
     example celecoxib, and a glycol ether, for example diethylene glycol
    monoethyl ether. At least a substantial part of the drug is in dissolved
     or solubilized form in a solvent liquid comprising the glycol ether.
     composition has rapid-onset properties and is useful in treatment of
     cyclooxygenase-2 mediated conditions and disorders, particularly pain.
     For relief of pain in headache or migraine, the composition can
    optionally be administered together with a vasodilator. Solubility of
     celecoxib and valdecoxib in various solvent liqs. was studied. A soft
     gelatin capsule contained celecoxib 200, Labrasol 280, diethylene glycol
    monoethyl ether 280, and propylene glycol laureate 140 mg.
    58-08-2, Caffein, biological studies 58-55-9, Theophylline, biological
IT
             69-89-6D, Xanthine, alkyl derivs. 83-67-0, Theobromine
     studies
     110-71-4, Ethylene glycol dimethyl ether 110-80-5, Ethylene glycol
    monoethyl ether
                     111-76-2, Ethylene glycol monobutyl ether 111-77-3,
    Diethylene glycol monomethyl ether 111-90-0, Diethylene glycol monoethyl
     ether
            111-96-6, Diethylene glycol dimethyl ether 112-36-7, Diethylene
     glycol diethyl ether
                           112-48-1, Ethylene glycol dibutyl ether
    Triethylene glycol dimethyl ether 112-50-5, Triethylene glycol monoethyl
            112-73-2, Diethylene glycol dibutyl ether
                                                        122-99-6, Ethylene
    glycol monophenyl ether 124-07-2D, Caprylic acid, glycerides
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Triethylene glycol monobutyl ether 143-24-8, Tetraethylene glycol dimethyl ether 334-48-5D, Capric acid, glycerides 622-08-2, Ethylene glycol monobenzyl ether 629-14-1, Ethylene glycol diethyl ether 764-99-8, Diethylene glycol divinyl ether 18912-80-6, Diethylene glycol monoisobutyl ether 37321-62-3, Propylene glycol laurate 63980-40-5 68958-64-5, Polyoxyethylene glyceryl trioleate 156259-68-6, Capmul mcm 162011-90-7, Rofecoxib 169590-41-4, Deracoxib 169590-42-5, Celecoxib 181695-72-7, Valdecoxib **202409-33-4**, Etoricoxib 212126-32-4 215123-80-1 247074-38-0 266320-83-6 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (rapid-onset formulation of selective cyclooxygenase-2 inhibitors) ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2000:314539 CAPLUS 132:329940 Pharmaceutical compositions containing histaminergic agonist and COX-2 inhibitor for migraine treatment Simitchieva, Kremena; Reines, Scott A.; Mckinney, Errol; Sandquist, Eric J.; Khanna, Deepak K.; Hargreaves, Richard Merck & Co., Inc., USA PCT Int. Appl., 16 pp. CODEN: PIXXD2 Patent English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ______ **___**____ ____ -----Al 20000511 WO 1999-US25388 19991029 <--WO 2000025779 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG CA 2348979 20000511 CA 1999-2348979 AA19991029 <--EP 1126841 EP 1999-960171 Α1 20010829 19991029 <--AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2002528498 20020903 JP 2000-579220 Т2 19991029 <--AU 759307 В2 20030410 AU 2000-17098 19991029 US 2002016348 Α1 20020207 US 2001-934823 20010822 <--US 6384034 В2 20020507 A1 US 2002177617 20020326 <--20021128 US 2002-106845

20010822 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 9 ALL CITATIONS AVAILABLE IN THE RE FORMAT

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19981102

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TIPharmaceutical compositions containing histaminergic agonist and COX-2 inhibitor for migraine treatment

PΙ WO 2000025779 Al **20000511**

PRAI US 1998-106605P P

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WO 1999-US25388

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PATENT NO. KIND DATE APPLICATION NO. DATE _____ ______ Al 20000511 WO 2000025779 PΙ WO 1999-US25388 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

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                                            US 2002-106845
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     A combination of a 5HT1B/1D agonist and a cyclooxygenase-2 (COX-2)
AΒ
     selective inhibitor is useful in the treatment and/or prevention of
     migraine. The 5HT1B/1D agonist is selected from sumatriptan,
     naratriptan, zolmitriptan, eletriptan, almotriptan, and rizatriptan, and
     the COX-2 inhibitor is selected from meloxicam, MK-663, Vioxx, RS 57067,
     celecoxib, and compound I. The 5HT1B/1D agonist and COX-2 inhibitor are
     administered combined in a single dosage form or as sep. dosage forms
     administered concurrently. Tablets containing 5 and 10 mg of rizatriptan
     benzoate and 10 mg Vioxx were prepared
ST
     cyclooxygenase inhibitor histaminergic agonist tablet migraine
IT
     5-HT agonists
        (5-HT1B; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     5-HT agonists
        (5-HT1D; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
IT
     Antimigraine agents
        (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
IT
     Drug delivery systems
        (tablets; tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
ΙT
     39391-18-9, Cyclooxygenase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (2, inhibitors; tablets containing histaminergic agonist and COX-2
        inhibitor for migraine treatment)
IT
     71125-38-7, Meloxicam 103628-46-2, Sumatriptan
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     Naratriptan
                  139264-17-8, Zolmitriptan 143322-58-1, Eletriptan
     144034-80-0, Rizatriptan
                               145202-66-0, Rizatriptan benzoate
     154323-57-6, Almotriptan
                                162011-90-7, Vioxx
                                                     169590-42-5, Celecoxib
     179382-91-3, RS 57067
                            180200-69-5 202409-33-4, MK 663
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (tablets containing histaminergic agonist and COX-2 inhibitor for
        migraine treatment)
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